IN THE CLAIMS:

Please amend claims 12, 20, and 21; cancel claims 1-11 and 23-26; and add new claims 27-30.

This listing of claims will replace all prior versions, and listings of the claims in the application.

Listing of the claims

1. – 11. **(Canceled).**

12. **(Currently amended)** A method of generating a microRNA comprising the steps of:

identifying a selected mRNA sequence to be the target of the microRNA;

generating an oligonucleotide ~~sequences~~ sequence that is 17-25 nucleotides and has a degree of complementarity to the selected mRNA sequence that is indicative of a microRNA-recognition element for a microRNA,

wherein the microRNA includes

a proximal region that is 7-9 nucleotides, has a 5' end and a 3' end and includes a nucleotide at the 5' end which is the microRNA's 5' terminus nucleotide,

a distal region that is 7-15 nucleotides, has a 5' end and a 3' end and includes a nucleotide at the 3' end which is the microRNA's 3' terminus nucleotide, and

a loop region that is 0 nucleotides ~~nucleotide~~, 2-3 nucleotides, or 6-9 nucleotides ~~nucleotide~~,

wherein when the loop region is 0 nucleotides, the 3' end of the proximal region is contiguous to the 5' end of the distal region, and when the loop region is 2-3 nucleotides or 6-9 nucleotides, the 3' end of the proximal region is contiguous to the 5' end of the loop region, and the 3' end of the loop region is contiguous to the 5' end of the distal region,

wherein complementarity of the mRNA sequence to the microRNA sequence that is indicative of a microRNA-response element for the microRNA is characterized by:

an mRNA sequence having a sequence that:

a) includes a region corresponding to the proximal region of the microRNA that is either; (i) completely complementary to the proximal region, or (ii) has a single mismatch (A) to the 5' end of the proximal region, or (B) symmetrically placed between the 5' end of the proximal region and the 3' end of the proximal region; and

b) includes a region corresponding to the loop region of the microRNA that either forms a loop of 2-5 non-paired nucleotides of mRNA when the loop region of the microRNA is 0, or has 0 nucleotides when the loop region of the microRNA is 6-9 nucleotides, or has 2-3 nucleotides which forms a bulge of 2-3 non-complementary nucleotides of mRNA ~~of the loop region~~ when the loop region of the microRNA is 2-3 nucleotides; and

c) includes a region corresponding to the distal region of the microRNA that is either; (i) completely complementary to at least 7 contiguous nucleotides of the distal region of the microRNA, including the 5' end of the distal region, or (ii) contains (A) mismatches of 1-4 contiguous nucleotides and (B) matches of at least 5 nucleotides to a contiguous nucleotide sequence of the distal region of the microRNA, including the 5' end of the distal region;

wherein the oligonucleotide sequence has a degree of complementarity to the selected mRNA sequence that is indicative of a microRNA for a microRNA-recognition element.

13. **(Original)** The method of claim 12 further comprising the step of determining free energy of the microRNA bound to the selected mRNA sequence wherein a free energy determination of -10 kcal/mole or less indicates that said mRNA sequence is a microRNA-recognition element for the microRNA.

14. **(Original)** The method of claim 12 wherein a free energy determination of -20 kcal/mole or less indicates that said mRNA sequence is a microRNA-recognition element for the microRNA.

15. **(Original)** The method of claim 12 wherein a free energy determination of -30 kcal/mole or less indicates that said mRNA sequence is a microRNA-recognition element for the microRNA

16. **(Previously presented)** The method of claims 12 wherein the selected mRNA sequence is a known MRE.

17. **(Previously presented)** The method of claims 12 wherein the selected mRNA sequence is in the 3' untranslated region of an mRNA.

18. **(Previously presented)** The method of claims 12 wherein an oligonucleotide is synthesized having the sequence of the generated microRNA.

19. **(Previously presented)** A system for identifying a microRNA-recognition element comprising:

an input interface for inputting mRNA sequences, a database of mRNA sequences or a link for connecting to a remote data input interface, data or a database of mRNA sequences;

an input interface for inputting microRNA sequences, a database of microRNA sequences or a link for connecting to a remote data input interface, data or a database of microRNA sequences;

a processor with instructions for comparing mRNA sequences to microRNA sequences to identify a microRNA-recognition element according to the method of claims 12.

20. **(Currently amended)** The system of ~~claims~~ claim 19 comprising a link for connecting to a database of mRNA sequences.

21. **(Currently amended)** The system of ~~claims~~ claim 19 comprising an input interface for inputting microRNA sequences.

22. **(Previously presented)** A computer program embodied on a computer readable medium for implementation on a computer system that for identifying a microRNA-recognition element, the program comprising instructions for performing the steps of the method of claims 12.

23. – 26. **(Canceled).**

27. **(New)** The method of claim 12, further comprising the step of synthesizing the oligonucleotide sequence and testing the function of the oligonucleotide to determine whether the oligonucleotide modulates the expression of the mNA.

28. **(New)** The method of claim 27, wherein the step of testing the function of the microRNA results in activation or inhibition of the expression of the mRNA by at least 10%.

29. **(New)** A method of preparing a microRNA comprising the step of:

confirming that a microRNA candidate oligonucleotide functions to inhibit expression of a selected mRNA sequence that is present in a cell by contacting the microRNA candidate oligonucleotide with the selected mRNA present in the cell and determining expression;

wherein said microRNA candidate oligonucleotide was produced by

a) identifying a selected mRNA sequence that is present in a cell to be the target of the microRNA candidate;

b) generating an oligonucleotide sequence of a microRNA candidate oligonucleotide, wherein the oligonucleotide sequence is

1) 17-25 nucleotides, and

2) has a degree of complementarity to the selected mRNA sequence that is indicative of a microRNA-recognition element for a microRNA,

wherein the 17-25 nucleotides of the microRNA candidate include

i) a proximal region that is 7-9 nucleotides, has a 5' end and a 3' end and includes a nucleotide at the 5' end which is the microRNA candidate's 5' terminus nucleotide,

ii) a distal region that is 7-15 nucleotides, has a 5' end and a 3' end and includes a nucleotide at the 3' end which is the microRNA candidate's 3' terminus nucleotide, and

iii) a loop region that is 0 nucleotides, 2-3 nucleotides or 6-9 nucleotides,

wherein

when the loop region of the microRNA candidate is 0 nucleotides, the 3' end of the proximal region is contiguous to the 5' end of the distal region, and

when the loop region of the microRNA candidate is 2-3 nucleotides or 6-9 nucleotides, the 3' end of the proximal region is contiguous to the 5' end of the loop region and the 3' end of the loop region is contiguous to the 5' end of the distal region,

and

wherein complementarity of the mRNA sequence to the microRNA candidate sequence that is indicative of a microRNA-response element for the microRNA candidate is characterized by an mRNA sequence having a sequence that:

i) includes a region in the mRNA sequence corresponding to the proximal region of the microRNA candidate that is either

A) completely complementary to the proximal region of the microRNA candidate, or

B) has a single mismatch to the 5' end of the proximal region of the microRNA candidate, or

C) has a single mismatch symmetrically between the 5' end of the proximal region of the microRNA candidate and the 3' end of the proximal region of the microRNA candidate;

ii) includes a region in the mRNA sequence corresponding to the loop region of the microRNA candidate that either

A) forms a loop of 2-5 non-paired nucleotides of mRNA when the loop region of the microRNA candidate is 0, or

B) has 0 nucleotides of mRNA sequence when the loop region of the microRNA candidate is 6-9 nucleotides, or

C) has 2-3 nucleotides in the mRNA sequence which form a bulge of 2-3 non-complementary nucleotides in the mRNA sequence when the loop region of the microRNA candidate is 2-3 nucleotides; and

iii) includes a region corresponding to the distal region that is either:

(A) completely complementary to at least 7 contiguous nucleotides of the distal region of the microRNA candidate including the 5' end of the distal region of the microRNA candidate, or

(B) contains (i) mismatches of 1-4 contiguous nucleotides of mRNA sequence and (ii) matches of at least 5 nucleotides of mRNA sequence to a contiguous nucleotide sequence of the distal region of the microRNA candidate including the 5' end of the distal region of the microRNA candidate;

and

c) synthesizing a microRNA candidate oligonucleotide having said oligonucleotide sequence.

30. **(New)** The method of claim 31 wherein contacting the microRNA candidate oligonucleotide with the selected mRNA present in the cell results in inhibition of the expression of the mRNA by at least 10%.